REMARKS/ARGUMENTS

Claims 11-20 are pending in the Application. Applicant respectfully requests entry of currently amended Claim 11 and new Claims 23-27.

Claim 11 has been amended to add the transitional phrase "consisting of" and exclude any ingredient not specified in the claim, i.e., to exclude ingredients other than the defined carrier and defined opioid analgesic. See MPEP 2111.03. Claim 11 has also been amended to change the average particle size of the carrier from a range of 60 to 100 μm to a range of 62 to 100 μm. New Claim 23 also includes the amended range. Support for the range average particle sizes for the carrier is found at pages 15-17, Examples 1-3, and page 11, 3rd ¶, pages 11-12, bridging ¶, and page 14, 2nd full ¶, of the Specification. New Claims 23-27 limit the average particle size of the opioid analgesic to "up to 20 μm," preferably "up to 10 μm." Support in the Specification for the opioid particle size is found at page 14, 2nd ¶. In addition, new Claim 23 employs the transitional phrase "consisting essentially of" which limits the claimed composition to the specified materials and those that do not materially affect the basic and novel characteristics of the claimed composition. See MPEP 2111.03.

No new matter has been added.

Rejection under 35 U.S.C. 112, 1st ¶ (written description)

Previously presented Claims 11-20 were rejected under 35 U.S.C. 112, 1st ¶ (written description). See Official Action, dated September 5, 2008 (OA, pp. 2-3). PTO finds no written description of an average particle size range of "60 μm to 100 μm" in the original Specification.

Support for the amended lower limit of the average particle size range of 62 μm for the carrier can be found in Examples 1-3 on pages 15 and 17 of the Specification. In each of Examples 1-3, the "carrier had an average particle size of about 62 μm." Support for the upper limit of the average particle size range of the carrier can be found in the "20 to 100

μm" range identified at page 11, 3rd ¶, pages 11-12, bridging ¶, and page 14, 2nd full ¶, of the Specification. According, a particle size range of 62 to 100 μm is described in the Specification as required by 35 U.S.C. 112, 1st ¶.

Persons having ordinary skill in the art would have understood that Applicant's specification describes a range of average particle sizes for the carrier of 62 to 100 μm. All that an applicant's specification is required to do to satisfy the written description requirement of 35 U.S.C. 112, 1st ¶, is to convey to persons having ordinary skill in the art with a reasonable degree of clarity that the applicant was in possession of the claimed subject matter. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Persons having ordinary skill in the art reading Applicant's Specification would have understood that carriers with an average particle size of 20 to 100 μm are preferred and that carriers with an average particle size of 62 μm are exemplified. Persons having ordinary skill in the art reasonably would have learned therefrom that Applicant's invention includes carriers with an average particle size of 62 μm to 100 μm.

Currently amended Claim 11 and new Claim 23 should be entered.

Rejection under 35 U.S.C. 103 over Yanagawa in view of Wermeling and "DIH"

Previously presented Claims 11-20 were rejected under 35 U.S.C. 103 over Yanagawa (U.S. Patent 5,603,943, patented February 18, 1997) in view of Wermeling (US Patent Application Publication 2003/0077300, published April 24, 2003) and Drug Information Handbook)(OA, p. 4). The rejection should be withdrawn.

Citing Yanagawa's claims and column 4, lines 28-44, of the patent, PTO finds (OA, p. 5; emphasis added):

> Yanagawa teaches that the physiologically acceptable substances that may be used with the nasally administrable carriers may be any that has a molecular weight less than 40,000 such as those that are employed as ordinary pharmaceuticals, for example, antiemetics (col. 4, lines 28-44).

PTO's findings are unreasonable.

Yanagawa requires that physiologically acceptable substances used with the nasally administrable carriers must be (1) "nasally administrable" (Yanagawa, col. 2, ll. 55-58), (2) homogenously absorbable on a polyvalent metal carrier (Yanagawa, col. 2, ll. 45-47), and, when absorbed on a polyvalent metal carrier and nasally administrated, (3) equally or more bioavailable when compared with the bioavailability of injected or orally administered physiologically acceptable substances (Yanagawa, col. 2, ll. 33-34). Yanagawa is particularly concerned with physiologically active peptides such as calcitonin and insulin (Yanagawa, col. 2, ll. 9-34). In the long list of physiologically active substances which Yanagawa states "may be . . . employed as ordinary pharmaceuticals" (Yanagawa, col. 4, ll. 28-67; emphasis added), there is not a single opioid analgesic mentioned. Contrary to PTO's finding, persons having ordinary skill in the art would not have considered opioid analgesics to be "ordinary pharmaceuticals" (Yanagawa, col. 4, l. 31). Yanagawa teaches (Yanagawa, col. 2, ll. 59-62; emphasis added), "The physiologically active substance to be used in the present invention may be any one of those employed as ordinary pharmaceuticals . . . ." Nor would persons having ordinary skill in the art have found other analgesics included in the long list of physiologically active substances mentioned by Yanagawa at column 5, line 5, to column 6, line 35.

In addition, Yanagawa contemplates a seemingly limitless scope of multivalent compounds such as aluminum compounds, calcium compounds, magnesium compounds, silicon compounds, iron compounds and zinc compounds as a carrier (Yanagawa, col. 2, l. 63, to col. 4, l. 26). Unlike Applicant, Yanagawa is not concerned with the carrier's effect on the administration of, and compatibility with, any particular kind of physiologically active substance other than peptides. See Yanagawa's Examples 1 (insulin with hydroxyapatite), 2-3 and 7 (salmon calcitonin with hydroxyapatite), 4 and 7 (salmon calcitonin with magnesium stearate), 5 (salmon calcitonin with calcium carbonate), 6 (salmon calcitonin with aluminum

hydroxide), 8 (glucagon with hydroxyapatite), 9 and 12 (glucagon with calcium carbonate), 10 (somatropin with hydroxyapatite or calcium carbonate), and 11 (somatropin with calcium lactate or calcium carbonate). In Example 7, Yanagawa tested different carriers for their ability to absorb salmon calcitonin. In Examples 8-12, Yanagawa tested different carriers for their ability to deliver specific physiologically active hormones to the blood. Certain specific carriers absorbed certain substances better than others. Certain specific carriers delivered certain substances to the blood more efficiently.

Persons having ordinary skill in the art would have understood from Yanagawa's disclosure that the substance-absorbability of any particular carrier and its ability to efficiently deliver a physiological substance to the blood by nasal administration depends on the specific carrier selected to absorb the substance and the kind of substance to be absorbed by the specific carrier. Finding an effective carrier for a specific kind and physical state of a physiologically active substance is no simple task. Various tests on animals are required. Moreover, for a physiologically active substances not mentioned or represented in any of Yanagawa's long lists thereof, persons having ordinary skill in the art would have expected the amount of experimentation required to find a suitable carrier for nasally delivering a different kind of physiologically active substance to be undue, i.e., undue experimentation would be required. Evidence that undue experimentation is required to find an effective carrier for a distinct kinds and phases of distinctly other substances is evidence in support of patentability, not obviousness.

Applicant's Specification teaches that carriers acceptable for one kind physiologically active substance could not be expected to be suitable for distinct substances with respect to absorbability, deliverability, and other properties. The Specification instructs (Spec., pp. 10):

> Use of a water soluble [carrier] has been deemed adequate in conventional intranasal formulations in view of the absorption of the effective ingredient in the body. However, according to the findings by the inventors of the present invention, a water soluble carrier is not necessarily favorable, and a carrier like calcium carbonate and/or

> calcium phosphate used in the present invention which becomes attached to the nasal mucosa without dissolving in water is capable of efficiently releasing the opioid analgesic to attain the biological absorption of the effective ingredient from the nasal mucosa.

To show that Yanagawa would have provided persons having ordinary skill in the art no more than an invitation to experiment with particulate carriers for opioids, Applicant's Specification compares some of Yanagawa's carriers (Spec., pp. 10-11, bridging ¶):

> Typical conventional carriers used include calcium carbonate, calcium phosphate, calcium lactate, calcium stearate, aluminum hydroxide, aluminum oxide, magnesium carbonate, and magnesium hydroxide. Of these carriers, calcium lactate becomes dissolved on the nasal mucosa, and calcium stearate turns into an oily form on the nasal mucosa, and these compounds are less adequate for use as a carrier. In addition, aluminum hydroxide, aluminum oxide, magnesium carbonate, and magnesium hydroxide are highly stimulative, and use of these compounds for the carrier in intranasal formulation may present various problems.

On the other hand, Applicant's experiments showed that calcium carbonate and calcium phosphate have (1) good affinity for opioid analgesics, (2) smooth attaching and releasing of the opioid analgesic, and (3) little stimulation for the nasal mucosa (Spec., p. 11, 1st ¶). Thus, PTO appears to have erred in concluding that it would have been obvious in view of Yanagawa's teaching to use any and all multivalent metal carriers to effectively deliver any and all physiologically active substances by nasal administration without undue experimentation.

To remedy Yanagawa's failure to mention opioid analgesics for nasal administration, PTO relies on the teaching of DIH and Wermeling. DIH recognizes that administration of opioids to a patient may cause nausea, and antiemetics were generally known to be administered to patients in need in combination along with opioids (OA, p. 5). Yanagawa's list of physiologically active substances includes antiemetics. However, Yanagawa's list of physiologically active substances does not include opioids and Applicant's claims are all closed to the addition of antiemetics. Accordingly, DIH does not remedy the deficiencies in Yanagawa's teaching.

Pressing on with no more guidance and instruction than Applicant's own Specification, PTO finds that Wermeling would have taught intranasal administration of opioids including fentanyl to persons having ordinary skill in the art (OA, p. 5). The problem with Wermeling's teaching, and PTO summarily dismisses the distinction, is that Wermeling teaches that opioids may be administered intranasally in the form of a liquid solution thereof. Wermeling teaches [0129], "Liquid formulations are prepared as fully dissolved solutions in a nasal carrier . . . ." At [0023; emphasis added], Wermeling teaches, "Compounds for use in the practice of the invention must be soluble in a pharmaceutically acceptable carrier that can be nasally administered . . . ." Wermeling's opioids include fentanyl [0022; 0129]. However, Wermeling acknowledges [0007], "No opioids or other controlled substances have heretofore been made available as intranasal formulations." Accordingly, where Wermeling states that the dose can also comprise microcrystalline particles of the pharmaceutically active composition in a form that is readily absorbable by the nasal mucosa [0019], Wermeling appears to be speculating outside the scope of its invention and the prior knowledge in the art. See Wermeling's claimed solutions. Patentability should never be resolved based on speculation. *In re Steele*, 305 F.2d 859, 862 (CCPA 1062).

Nervertheless, PTO finds that DIH and Wermeling transform Yanagawa's invitation to experiment into a reasonable suggestion to do what Applicant has done, to find what Applicant's have found, and to do everything without undue experimentation. Based on DIH, PTO summarily finds that opioid analgesics are "ordinary pharmaceuticals" (OA, p. 6). Based on Wermeling, PTO finds that persons having ordinary skill in the art would have known that opioid analgesics can be administered intranasally (OA, p. 6). Accordingly, PTO concludes that it would have been obvious for a person skilled in the art to administer opioid analgesics by the method Yanagawa teaches without undue experimentation with reasonable expectation of success (OA, pp. 6-7).

PTO summarizes its position as follows (OA, p. 6; emphasis added):

> At the very least, the incorporation of a conventional opioid analgesic into Yanagawa's compositions would have been obvious to try, because opioids are ordinarily employed pharmaceuticals; are known to be nasally administrable (Wermeling), and thus the ordinary skilled artisan would have had a reasonable expectation of predictability of successfully administering an opioid analgesic (e.g. fentanyl) using Yanagawa's modified composition.

PTO's conclusions are more remarkable for what they do not say than for what they say. There is no recognition in the applied prior art that opioid analgesics in solid form, particulate, powder or otherwise, were known to be nasally administrable or reasonably would have been expected to be nasally administrable. There is no mention of Yanagawa's suggestion that undue experimentation would have been required to find effective carrier's for nasal administration of a wide variety of functionally and chemically distinct physiologically active substances, more specifically opioid analgesics in solid form. There is no mention of Applicant's uncontested findings that few of Yanagawa's acceptable carriers are unsuitable for nasal administration of opioid analgesics. There is no mention of Applicant's uncontested findings that few of Yanagawa's acceptable carriers will attach opioids. There is no mention of Applicant's uncontested finding that water-soluble carriers or carriers soluble in nasal mucosa are unsuitable. There is no recognition that opioid analgesics attached to calcium carbonate and/or calcium phosphate carriers could be nasally administered with results at least equivalent to injected opioid analgesics or orally administered opioid analgesics. Finally, there is no acknowledgment of Wermeling's contrary teaching that opioids must be in solution to be nasally administered with any expectation of success.

Finally, PTO argues that "obvious-to-try" alone may be sufficient basis for concluding that Applicant's claimed composition is unpatentable under 35 U.S.C. 103. The Federal Circuit has denounced that argument. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). A reasonable suggestion to do what Applicant has done with some reasonable

expectation of success is the requisite basis for a conclusion of obviousness under 35 U.S.C. 103. PTO's rejection should be withdrawn.

Obviousness-type double patenting rejection over Yanagawa's claims, Wermeling, and DIH

Claims 11-20 were rejected for obviousness-type double patenting of Claims 1-2, 4, and 9-14 of Yanagawa (U.S. Patent 5,603,943, issued February 18, 1997) in view of Wermeling and DIH.

Yanagawa is prior art under 35 U.S.C. 102(b). Accordingly, the rejection of Applicant's claims over Yanagawa's claims are subsumed by the standing rejection over the Yanagawa's patent-in-full under 35 U.S.C. 103. Accordingly, the obviousness-type double patenting rejection should be moot.

Applicant's proposed amendment to Claim 11 and new Claims 23-27 should be entered to place the claims in condition for allowance or better condition for appeal. The amended and new claims are in condition for allowance. Entry and allowance are earnestly requested.

Respectfully submitted,

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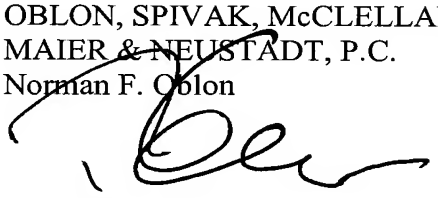

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